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(54) **[Title of the invention]** Hydrophilic pressure sensitive adhesive composition and biomedical electrode comprised of its composition

(57) **[Extent of the Claims]**

[Claim 1] A hydrophilic, pressure sensitive adhesive composition composed of a crosslinked, swellable type polymeric matrix formed by free radical polymerization of at least one polymerizable monomers species wherein a majority of the monomeric component is comprised of one or more N-vinyl lactams, and a crosslinking agent which is a multi-ethylenically unsaturated compound of which ethylenic groups are vinyl groups, allyl groups, and/or methallyl groups, which are bonded to nitrogen or oxygen atoms and a plasticizer

and above mentioned pressure sensitive adhesive composition characterized by the

plasticizer wherein the plasticizer of above mentioned crosslinking agent is present in an amount sufficient for the composition to be cohesive, swellable and pressure sensitive adhesive.

[Claim 2] A composition described in Claim 1 wherein above described multi-ethylenically unsaturated compound is chosen from the group of divinyl, diallyl or dimethallyl ester, divinyl which includes bis (N-vinyl-lactam) diallyl or dimethallyl amide, divinyl, diallyl or dimethallyl ether and divinyl, diallyl or dimethally urea

[Claim 3] A composition described in Claim 1 or 2 wherein drug is mixed with above described pressure-sensitive adhesive composition to form percutaneous drug delivering adhesive

[Claim 4] A composition described in Claim 1 or 2 in which above mentioned plasticizer is containing water and sufficient amount of electrolyte to be sensitive enough to allow the passing of the electric current

[Claim 5] A hydrophilic, pressure sensitive adhesive composition composed of a crosslinked, swellable type polymeric matrix formed by free radical polymerization of at least one polymerizable monomers species wherein a majority of the monomeric component is comprised of one or more N-vinyl lactams, and a crosslinking agent which is a multi-ethylenically unsaturated compound of which ethylenic groups are vinyl groups, allyl groups, and/or methallyl groups, which are bonded to nitrogen or oxygen atoms and a plasticizer

and a manufacturing method of hydrophilic pressure sensitive adhesive composition wherein above mentioned crosslinking agent and above mentioned plasticizer are existent in an amount sufficient for the composition to be cohesive, swellable and pressure sensitive and

the manufacturing method wherein

(a) a mixture is prepared comprising an N-vinyl lactam monomer, a multi-ethylenically unsaturated crosslinking compound in which the ethylenic groups are vinyl groups, allyl groups or methallyl groups bonded to nitrogen or oxygen atoms, a plasticizer which is a solvent for the above mentioned N-vinyl lactam monomer and above mentioned multi-ethylenically unsaturated compound and a free radical initiator;

(b) a layer is formed by depositing the above mentioned mixture on the substrate and

(c) the above mentioned layer is exposed to sufficient energy to form swellable, cohesive and crosslinked copolymer.

[Claim 6] Biomedical electrode which contains an electrical conductor having means for connecting to a lead wire of electromedical device and which is formed of hydrophilic pressure sensitive adhesive comprising a crosslinked, swellable type polymeric matrix formed by free radical polymerization of at least one polymerizable monomers species wherein a majority of the monomeric component is comprised of one or more N-vinyl lactams, and a crosslinking agent which is a multi-ethylenically unsaturated compound of which ethylenic groups are vinyl groups, allyl groups, and/or methallyl groups, which are bonded to nitrogen or oxygen atoms and a plasticizer, and above mentioned plasticizer and above mentioned crosslinking agent are existent in an amount sufficient for the composition to be cohesive, swellable and pressure sensitive and

characterized by that above mentioned plasticizer contains water and contacts hydrophilic pressure sensitive adhesive composition having further electrolyte in an amount sufficient to make the composition sensitive to the passing of electric current.

[Detailed description of the invention

Field of this invention

This invention relates to compositions comprised of a crosslinked hydrophilic polymer which are useful compositions for pressure sensitive adhesives. One form of this invention relates to a composition which is made to be electrically-conductive for the use as skin interfacing material in a disposable bio-electrode. In its preferred embodiment, the invention relates to pressure sensitive adhesives made with N-vinyl-2 pyrrolidone crosslinked with controlled amounts of specific crosslinking agents.

Background of the invention

Adhesives that can be incorporated with substantial amount of water or other polar liquid without unacceptable phase separation, loss of tackiness or loss of cohesive strength are in demand in variety of applications. If such adhesive is made electronically conductive, it would be specifically useful as bio-medical electrode. An adhesive

that can be made electrochemically reactive and used with galvanically inert graphite conductors to make a bio-electrode that can recover from polarizing overloads is not known.

Many adhesives for medical use are known. Examples are polyvinyl ethers and copolymers of hydrophobic water insoluble monomers such as isooctyl acrylate and a small amount of a water soluble monomer such as a short chain α,β-unsaturated carboxylic acid (e.g. acrylic acid) or an N-vinyl lactam (e.g. N-vinyl-2-pyrrolidone). While those formulations make excellent medical adhesives, incorporation of substantial amounts of ionic or highly polar solutions causes phase separation.

Conductive adhesives have been known for many years. U.S. Patent No. 4,066,078 (issued to Berg), U.S. Patent Nos. 4,273,135 and 4,352,359 (both issued to Larimore et al.) and U.S. Patent Nos. 4,524,087, 4,539,996 and 4,554,924 (all issued to Engel) are representative examples. Berg discloses two classes of conductive adhesive plasticized with a polyhydric alcohol. One is a polymer or copolymer derived from the polymerization of an ester of an olefinically unsaturated carboxylic acid and a mono- or polyhydric alcohol having a terminal quaternary ammonium group. The second one is sulfated cellulose esters. The manufacturing process for both classes are cumbersome using multiple steps.

Each patent of Larimore et al. shows three classes of polymers for use in conductive adhesives.

U.S. Patent No. 4,273,135 describes the first class which is comprised of non-ionic water soluble homo-or copolymers of substantially, totally water soluble monomers. The second and third classes are copolymers of water soluble monomers and water insoluble monomers, the third class requires its polymer to be water insoluble and at least 15% of the monomers to be water soluble. In U.S. patent No. 4,352,359 carboxylate containing monomers are needed. Although the electrical properties of these adhesives are suitable for some applications, cross linking is not disclosed. For cross linking, relatively large amount of polyhydric alcohol can be used without reducing the viscosity below the acceptable level.

Two Engel Patents (U.S. Patent Nos 4,524,087 and 4,539,996) disclose an electrically conductive adhesive formed by and essentially solventless free radical polymerization of an adhesive precursor having a polyhydric alcohol, at least one kind

of ionic monomer, a cross linking agent and an initiator. The ionic monomers listed are salts of α,β-unsaturated carboxylic acids. The third Engel patent (U.S. Patent No. 4,554,924) discloses a conductive adhesive formed by an essentially solventless free radical polymerization of an adhesive precursor having a polyhydric alcohol, at least one non-ionic monomer, an initiator, a cross linking agent and an ionizable salt being present in an amount sufficient to render the composition electrically conductive. One example describes a precursor comprising 115 g N-vinyl-2-pyrrolidone, 0.3 g triethylene glycol-bis-methacrylate, benzil-dimethylketal (Irgacure TM 651, Ciba Geigy), 25.0 g water, 250 g glycerol, 17.1 g potassium chloride and 36.0 g polyacrylic acid solution (sodium salt in water (50% by weight)). The obtained adhesive is highly tacky but it is stringy, and shows poor cohesion so that it leaves a substantial residue when removed.

The preferable Engel adhesives are used in various bio-medical electrodes. These adhesives are lightly cross linked polymers of acrylic acid in glycerol which contains water and *sodium chloride. Although, these show good properties in a few applications, it is not possible to optimize electrical properties without giving disadvantageous effect to the adhesive property. Experience shows that increasing the water content of the composition virtually improves the property of electrode coated by the adhesive. Unfortunately, increasing the water content to the optimum levels for electrical property results in initial tackiness and cohesive strength of the polymer are reduced, adhesion to the skin becomes poor and residue is found when the electrode is removed.

Tackifier can be used, however this does not contribute to optimization of electrical property and adhesion. In addition to this, long time storage (for more than 2 years) results in the loss of tackiness. This is believed to be due to the esterified crosslinking of polymeric chains.

Other conductive adhesive is disclosed in U.K. Patent application No. 2,115,431. The adhesive is composed of at least one kind of irradiation cross linked organic polymer and an adhesive plasticizer. Crosslinked polymer is formed by radiating the ionizing radiation energies (e.g., x-ray, γ-ray and electron beam irradiation) which is equivalent to at least 100,000 electron volts, to at least one kind of uncrosslinked synthetic organic polymer (includes one which has repeating units derived

from an N-vinyl lactam monomer). Using ionizing irradiation to promote chemical reactions is very useful in many applications, however those in the industry must have confirmed that the use of ionizing irradiation is not always desirable because the use of ionizing irradiation makes the control of the process very difficult and wide range of reactive species are formed which make predicting the effect of additional constituent very difficult.

Another technology which involves polymer matrix which swells in the water is hydrogel technology. These compositions are covalently crosslinked and are used widely in the contact lens. Many of these hydrogels are based on poly (N-vinyl-2 pyrrolidone) and widely used in the medical applications. As the safety of poly (N-vinyl-pyrrolidone) in medical application is publicly known from a long time experience, it is one of the desired candidate for bio-compatible adhesives. Most of the hydrogels are not adhesive, however, EPO Application No. 83305770.6 (Publication 0107376, 02/05/84) describes a hydrogel having some tackiness and which is recommended for the use as wound dressing. This hydrogel is prepared by dissolving the poly (N-vinyl-pyrrolidone) at between 15 to 25 weight percent into water and crosslinking with ionizing irradiation (1 - 5 Mrads, electron beam). Ionizing irradiation is not desirable in this case neither.

Polymer matrix which use multifunctional monomer to crosslink N-vinyl lactam is publicly known in the document. However, adhesive is not found.

U.S. Patent No. 3,294,765 discloses crosslinked polymer matrix of N-vinyl lactam which is crosslinked with 3.3'-ethylidene-bis (N-vinyl-pyrrolidone). In this patent, a polymer matrix with a mechanical property in which the range of gel changes from thickened solution to intractable gel depending on the amount of crosslinking agent is described. There is no report regarding the adhesive.

U.S. Patent No. 4,536,554 discloses polymeric network structured mixture of a polymer formed from hydrophilic monomer N-vinyl-2 pyrrolidone and hydrophobic monomer (5-alkylene-m-dioxanyl) acrylic ester. Crosslinking agent listed as suitable for N-vinyl-2-pyrrolidone includes 3.3'-ethylidene-bis (N-vinyl-2-pyrrolidone) and a variety of other diallyl, dimethallyl and divinyl multifunctional monomers. As the polymeric network structure is used for contact lenses, adhesive characteristic does not seem to be desirable.

The polymeric composition known publicly in this industry did not meet the requirement for an N-vinyl lactam based pressure sensitive adhesive which can allow incorporation of water and other polar liquid (particularly glycerol). There is still a need of adhesive suitable to use in biomedical electrode which maintains the function after a long period of storage. Also, an adhesive which shows no biocompatibility problems and can be manufactured by a simple process is needed.

Summary of the invention

It was a surprise that an excellent pressure sensitive adhesive was found to have been formed which allows incorporation of substantial amount of water, other polar liquid and ionic species to partially swelled gels derived from N-vinyl lactam and suitable crosslinking agent. This invention is a hydrophilic, pressure-sensitive adhesive composition comprising a crosslinked, cohesive swellable polymeric matrix and a solution for plasticizing purpose. The crosslinked, cohesive and swellable polymer matrix is formed by free radical polymerization of a precursor having monomer species and a crosslinking agent. When the majority of monomer species is N-vinyl-lactam, the obtained adhesive can contain substantial amount of polar liquid and ionic species. Although variety of crosslinking agent can be used for the crosslinking of N-vinyl-lactam, a multi-ethylenically unsaturated compound wherein the ethylenic groups are vinyl, allyl or methallyl groups bonded to nitrogen or oxygen atoms is used in this invention. the crosslinking agent and plasticizer exist in sufficient and controlled amount to form pressure sensitive swellable matrix.

The N-vinyl lactam which constitutes a majority of the monomer portions of the precursor can be selected from the following group of examples.

N-vinyl-2-pyrrolidone;

5-methyl-N-vinyl-2-pyrrolidone;

5-ethyl-N-vinyl-2-pyrrolidone;

3.3' dimethyl-N-vinyl-2-pyrrolidone

3-methyl-N-vinyl-2-pyrrolidone;

3-ethyl-N-vinyl-2-pyrrolidone;

4-methyl-N-vinyl-2-pyrrolidone;

4-ethyl-N-vinyl-2-pyrrolidone;

N-vinyl-2-valerolactam;
N-vinyl-2-caprolactam; and mixtures of any of the foregoing. Preferably, N-vinyl-lactam is N-vinyl-2-pyrrolidone. A comonomer such as N-N-dimethylacrylamide can be used. While other comonomers can be used without adverse effect, the majority of the monomer of this invention is an N-vinyl-lactam.

The crosslinking compounds which were found to be preferable in this invention are multifunctional and have vinyl groups, allyl groups and (or) methallyl groups bonded to nitrogen or oxygen atoms. The examples of the compound are divinyl, diallyl or dimenthally esters (e.g., divinyl succinate, divinyl adipate, divinyl maleate, divinyl oxalate, divinyl malonate, divinyl glutarate, diallyl itaconate, diallyl maleate, diallyl fumarate, dially diglycolate, diallyl oxalate, diallyl adipate, diallyl succinate, diallyl azelate, diallyl malonate, dially glutarate, dimethallyl maleate, dimethallyl oxalate, dimethallyl malonate, dimethallyl succinate, dimethallyl glutarate, and dimethallyl adipate), divinyl, diallyl or dimethallyl ethers (e.g., diethyleneglycol divinyl ether, butanediol divinyl ether, ethylene glycol divinyl ether, ethylene glycol diallyl ether, diethylene glycol diallyl ether, butane diol diallyl ether, ethylene glycol dimethallyl ether, diethylene glycol dimethallyl ether and butanediol dimethallyl ether), divinyl, diallyl or dimethallyl amides including bis (N-vinyl lactams), (e.g., 3,3'ethylidene bis (N-vinyl-2-pyrrolidone)) and divinyl, diallyl or dimethallyl ureas. Presently preferred crosslinking compounds are divinyl adipate, 3.3'-ethylidene bis (N-vinyl-2-pyrrolidone) and diethyleneglycol divinyl ether.

The preferred form of the adhesive compound is swellable, cohesive crosslinked polymeric matrix prepared by free radical polymerization of a precursor comprising N-vinyl-2-pyrrolidone monomer and less than 0.5 % (by weight of the monomer) of 3.3'-ethylidene bis (N-vinyl-2-pyrrolidone) and a plasticizer containing a mixture of glycerol and water.

Another form of this invention is relating to polymerizing precursor useful in manufacturing hydrophilic, pressure sensitive adhesive compositions comprising a mixture of an N-vinyl lactam monomer as the major monomer component, a plasticizer, a multi-ethylenically unsaturated compound in which the ethylenic groups are vinyl, allyl and/or dimethallyl* groups which are bonded to nitrogen or oxygen atoms and a free radical initiator.

This invention relates to the manufacturing of the adhesive compositions of this invention which further contain electrolyte in an amount sufficient to make the adhesive sensitive to the passing of electric current and biomedical electrodes of such conductive adhesive. Disposable biomedical electrode can be manufactured by this invention. This electrode comprises an electrical conductor, means for connecting the electrical conductor to a lead wire of an electromedical device and an electrically conductive pressure sensitive adhesive as described above. Majority of the surface of conductive body contacts the adhesive.

Adhesive articles such as medical tapes and bandages which used the adhesive composition of this invention are other characteristics of this invention.

Biomedical electrode and electrically conductive adhesive composition by this invention provide some advantages over the above described biomedical electrode. Firstly, using an N-vinyl lactam such as N-vinyl-2-pyrrolidone as the majority of monomer and one or more of the multi-ethylenically unsaturated crosslinking compounds described above enables adhesives to have excellent adhesion, cohesion, compliance and elasticity which is required in pressure sensitive adhesives. Especially, cohesion of the adhesive enables clean release from the skin. Glycerol which is an excellent humectant in the biomedical application can be used. Furthermore, hydrophilic polymer of this invention has an excellent shelf life unlike hydrophilic polymer based on acrylic acid. This improved shelf life is believed to result from eliminating the tackiness or delaying the reaction speed of reducing the tackiness by crosslinking the polymer between polyol and the lactam.

This invention relates to a method of manufacturing an adhesive composition as described above by:

(a) preparing a precursor comprising an N-vinyl lactam monomer, a multi-ethylenically unsaturated crosslinking compound in which the ethylenic groups are vinyl groups, allyl groups or methallyl groups bonded to nitrogen or oxygen atoms, a plasticizer which is also a solvent for the N-vinyl lactam monomer and the multi-ethylenically unsaturated compound and a free radical initiator;

(b) forming a layer by depositing the mixture on the substrate and

(c) exposing the layer to sufficient energy to initiate a free radical polymerization and characterized by the presence of sufficient amount of above mentioned multi-

ethylenically unsaturated compound and the plasticizer which form swellable and cohesive polymer matrix which is a pressure sensitive adhesive. By using a plasticizer as a solvent for N-vinyl lactam monomer and multi-ethylenically unsaturated cross linking agent, this method does not require the removal of the solvent from the adhesive after the polymerization of the monomer, the manufacturing method of the adhesive of this invention is essentially solvent-free.

Detailed explanation of this invention

The pressure sensitive adhesive compositions of this invention are obtained by the free radical polymerization either in bulk or in solution of a precursor containing an N-vinyl lactam monomer and a compound for crosslinking. The polymer can be dried then swelled with the plasticizer and is made into a pressure sensitive adhesive. Preferably, the plasticizer is mixed into the precursor in order to avoid the need of swelling by the evaporation of solvent and subsequent plasticizer.
Following is a list of examples of N-vinyl lactam which can be employed.
N-vinyl-2-pyrrolidone;
5-methyl-N-vinyl-2-pyrrolidone;
5-ethyl-N-vinyl-2-pyrrolidone;
3.3' dimethyl-N-vinyl-2-pyrrolidone
3-methyl-N-vinyl-2-pyrrolidone;
3-ethyl-N-vinyl-2-pyrrolidone;
4-methyl-N-vinyl-2-pyrrolidone;
4-ethyl-N-vinyl-2-pyrrolidone;
N-vinyl-2-valerolactam;
N-vinyl-2-caprolactam

The amount of N-vinyl lactam monomer in the polymerizable compositions of this invention is generally from 5 to 50 weigh percent of the precursor and preferably about 25 to 35 weight percent of the precursor. The N-vinyl lactam monomer (or a mixture of N-vinyl lactam) constitutes a majority of the monomers existent in the precursor. Preferably, N-vinyl lactam monomer constitutes 70 to 100 weight percent of the noncrosslinking monomers existent in the precursor and most preferably, 90 to 100 weight percent. For example, small amount of monomers soluble in the precursor

such as acrylic acid, methacrylic acid or hydroxyethyl methalcrylate may be included in the precursor. The most preferred pressure sensitive adhesives are obtained when entire noncrosslinking monomer is virtually N-vinyl-2-pyrrolidone.

The precursor further contains a "compound for crosslinking" which is a multi-ethylenically unsaturated compound wherein the ethylenic groups are vinyl groups, allyl groups or methallyl groups wherein groups are bonded to nitrogen or oxygen atoms. (The terms used in the detailed explanation of the invention, "vinyl group, allyl group and methallyl group" include substituted groups as well; for example, the term "vinyl groups "includes isopropenyl groups.) Although most of the easily available crosslinking compounds contain ethylenic groups from only one of the previous categories, it should be understood that the crosslinking compounds which have more than one of the previous ethylenic categories are also suitable. The exact range for the optimum performance might vary depending on the specific compound used, it has been found that relatively lower amount of crosslinking compound is very tacky and yet suitable to obtain an adhesive with good release from the skin. The crosslinked polymer matrix in the adhesives of this invention has been found to be stable for a long time storage. Although not limited by any theory, no more crosslinking of copolymer is believed to occur during the long time storage or use of adhesive under the ambient condition. This adhesive is also very hydrophilic and easily absorb and hold water and water soluble substance.

The crosslinking compounds which were found to be preferable in this invention are multifunctional and have vinyl groups, allyl groups and (or) methallyl groups bonded to nitrogen or oxygen atoms. The examples of the compound are divinyl, diallyl or dimenthally esters (e.g., divinyl succinate, divinyl adipate, divinyl maleate, divinyl oxalate, divinyl malonate, divinyl glutarate, diallyl itaconate, diallyl maleate, diallyl fumarate, dially diglycolate, diallyl oxalate, diallyl adipate, diallyl succinate, diallyl azelate, diallyl malonate, dially glutarate, dimethallyl maleate, dimethallyl oxalate, dimethallyl malonate, dimethallyl succinate, dimethallyl glutarate, and dimethallyl adipate), divinyl, diallyl or dimethallyl ethers (e.g., diethyleneglycol divinyl ether, butanediol divinyl ether, ethylene glycol divinyl ether, ethylene glycol diallyl ether, diethylene glycol diallyl ether, butane diol diallyl ether, ethylene glycol dimethallyl ether, diethylene glycol dimethallyl ether and butanediol dimethallyl

ether), divinyl, diallyl or dimethallyl amides including bis (N-vinyl lactams), (e.g., 3,3'ethylidene bis (N-vinyl-2-pyrrolidone)) and divinyl, diallyl or dimethallyl ureas. Presently preferred crosslinking compounds are divinyl adipate, 3.3'-ethylidene bis (N-vinyl-2-pyrrolidone) and diethyleneglycol divinyl ether.

Bis (N-vinyl-lactam) can be used at a lower level than a kind having a crosslinking agent. For example, multifunctional crosslinking agents such as tri or tetra functional compounds can be used as well, trivinyl glyceryl ether is an example. Such agents can be used in a slightly less amount than bifunctional crosslinking agents. However, multifunctional acrylate compounds were found to be not suitable when N-vinyl lactam comprises the majority of the monomers in the adhesive of this invention.

The amount of crosslinking compound in the adhesive of this invention should be generally between about 0.02 to about 5.0 weight percent of the N-vinyl lactam monomer in the composition. Generally these amounts provide desirable crosslinking to the pressure sensitive adhesive. However, different kind of compound is preferably used in the different level. Bis (N-vinyl lactam), other divinyl amides and divinyl ureas are preferably used at the amount from about 0.02 to about 0.5 weight percent of the polymer. Divinyl ethers are preferably used at the amount from about 0.5 to about 5 weight percent of the polymer. Divinyl, diallyl or dimethallyl esters, diallyl or dimethallyl ethers, diallyl or dimethallyl amides and diallyl or dimethallyl ureas are preferably used at the amount of from about 0.05 to about 2 weight percent of the polymer. The composition of this invention can be optimized by varying parameters such as the amount of light used to initiate polymerization, the amount of the initiator, temperature and the ratio of reactants.

The compositions of this invention contain plasticizer for crosslinking polymer. Preferred plasticizers are glycerol and mixtures of glycerol and water. Glycerol is the preferred plasticizer of this invention because it provides a composition which gives good adhesion to the skin, functions as a humectant to prevent excessive evaporation of moisture from the final composition and it is less stimulating than other polyol plasticizers such as ethylene glycol, propylene glycol. However, other polyol and alcohol (e.g., methanol, ethanol and isopropanol), ether alcohol (e.g., glycol ethers and polyethylene glycol) and any other publicly known plasticizers which can

swell polymer *atrix (matrix?) and does not cause skin irritation, can be used solely or in a mixture with glycerol or any other plasticizer compound. Other publicly known plasticizer may be used in other applications such as non medical field where toxicity and flammability are not concerns.

The plasticizer is added in the amount sufficient enough to render crosslinking copolymer into pressure sensitive adhesive. In general, the amount of plasticizer should be in the range from about 35 to about 95 weight percent of the adhesive composition, preferably from about 50 percent to about 90 weight percent. Glycerol is used up to the amount of 100 % of the plasticizer, preferably between 10 to 80 %. When the adhesive compositions of the invention are used in bioelectrodes, water is used in concentration rate from about 20 to 100 weight percent of the plasticizer, preferably at least about 30 weight percent.

Additives can be incorporated as well. For example, when adhesive is used as an electrode, water and electrolyte may be added to a precursor or a final composition. When additive interferes the polymerization or is affected by polymerization, the additive may be added after the polymerization. Ionic salts dissolved in the compositions in order to provide conductivity can be the ionic salts used generally by people in the industry for this purpose, such as lithium chloride, sodium citrate and preferably potassium chloride. Also, a redox couple which is a mixture of ferric and ferrous salts such as sulfates or gluconates may be added. The amount of ionic salts are relatively small, from about 0.5 to 10 weight percent of the adhesive and preferably 1 to 4 %. When a redox couple such as ferric and ferrous sulfates for example is used, electrode can recover from an overload potential. An electrochemically inert sensing element which is disclosed in Patent No. (blank) applied at the same date, can be used. This patent application can be a reference of this detailed description.

The adhesive composition of this invention can be used in the drug delivery system such as percutaneous drug delivery system. In such instance, the drug to be delivered can be incorporated to the adhesive during the preparation. For example, if the drug is not adversely affected by the polymerization, it can be mixed in polymerizable composition before the polymerization. Otherwise, it can be mixed with the adhesive after polymerization.

Polymerization of polymer precursor can be carried out by employing an

initiator which generate useful free radicals by applying activating energy such as those conventionally used in the polymerization of ethylenically unsaturated monomers. Thermally activated initiators such as organic peroxides, organic hydroperoxides and azo compounds are included in the useful free radical initiator. Representative examples of such initiators are benzoyl peroxide, t-butyl perbenzoate, diisopropyl peroxydicarbonate, cumene hydroperoxide, azobis (isobutyronitrile). Generally, from about 0.1 to 5 weight percent (based on the polymerizable components) thermal initiator is used. When thermally activated initiators are employed, polymerization is carried out at between about 40° to 100° C for about 5 to 500 minutes depending on the temperature and composition of polymerizable composition.

However, the present preferred polymerization initiators is the one activated photochemically. Such photochemically activated initiators are publicly known, there is a description in the document of polymerization, for example chapter 11 of "Photochmistry "John Wiley and Sons by Calvert and Pitts (1966) and in "Progress in Organic Coatings" 13 (1985) 123-150. Representative examples of such initiators are acyloins related compounds such as benzoin, benzoin methyl ether, benzoin ethyl ether, benzoin isopropyl ether, benzoin isobutyl ether, α-methylbenzoin and 2-hydroxy-2-methyl-1-phenyl-1-propanone and benzilketals such as benzildimethylketal and benzildiethylketal. A presently preferred photoinitiator is 2-hydroxy-2-methyl-1-phenyl-propanone.

Generally, the photo initiator is used in amount ranging from about 0.01 to 5 weight percent of the monomer. Preferably, about 0.02 to 2.0 weight percent photo initiator is used. When activating energy is ultraviolet light, it is initiated typically by the radiation at the temperature between 0° and 50° and for the duration of between 0.5 minutes and 5 hours or more depending on the intensity of the radiation and the opacity of the adhesive.

Other method of initiating free radical is publicly known and may be used in the application of this invention. For example, a system which include chemical reaction of two or more compounds which produce free (radical) initiator can be employed.

There are several methods in manufacturing pressure sensitive adhesives

of this invention. One variation includes polymerization of polymer precursor in bulk or solution with or without the presence of plasticizer. It is preferable to prepare the adhesive by an essentially solventless process of polymerizing the precursor comprising N-vinyl lactam monomer, crosslinking agent, initiator and plasticizer in which the monomer and crosslinking agent are soluble. Otherwise, a solvent can be added in order to facilitate mixing and polymerization of the mixture then removed by evaporation for example. The precursor is coated on an electrode plate or a transfer sheet and exposed to sufficient heat or actinic radiation energy to form swellable, cohesive crosslinking copolymer by a free radical initiator. The thickness of adhesive layer is generally about 5 to 100 mil (0.13 to 2.54 mm) and the preferable thickness is about 35 mil (0.89 mm).

Following is the explanation by referring to the attached drawings for a better understanding of the bioelectrode of this invention.

Referring to Fig 1, a disposable ECG electrode is shown in which electrically active conductor 12 is provided by a film 14 of approximately 3/16 inch diameter which is vapor coated with silver 16 on its lower surface. A standard stud/eyelet connector which is used to connect to the electrode of the electro medical equipment such as electrocardiogram, contacts electronically active conductor 12. In the example as shown, stud 18 is made of stainless steel and eyelet 20 is made of plastic having a conventional silver/silver chloride coating. An ionic salt (refer to application example 24) is incorporated in conductive adhesive layer 22. This is approximately 28 mil thick and covers the lower surface of conductor 12 contacting the skin. A release liner 24 protects conductive adhesive before the use.

The electrode 26 of Fig 2 and 3 is made of circular piece of standard medical pressure sensitive adhesive tape 28 such as Micropore TH tape sold by 3M Company, Saint Paul, Minn. Adhesive tape 28 is laminated to a disc of tin foil 30 which is approximately 1.7 mil thick and 1/4 inch diameter. Foil disc 30 constitutes the electrical connector of the electrode. Tab 32 extends from tape 28 and tin foil disc 30 and provide a means to connect the electrode plate to an electrocardiograph by using alligator clamp (not shown) or other suitable connector. Tab 32 is reinforced with a piece of polyethylene 34 (preferably colored) so that it is easily visible to the user. Conductive adhesive layer 38 is about 28 mil thick and applied to the lower surface of

the tin foil disc 30 where it contacts skin. Release liner 38 is used to protect adhesive before the use.

The following application example explain the adhesive of this invention. All the parts are in weight parts. The crosslinking agents are listed in the following.

Crosslinking agent	Compound
A	diethylenglycol divinyl ether
B	butanediol divinyl ether
C	divinyl adipate
D	3.3'-ethylidene bis (N-vinyl-2-pyrrolidone)
E	pentaerythritol diacrylate
F	triethyleneglycol dimethacrylate
G	ehtyleneglycol dimethacrylate
H	diallyl maleate
I	diallyl succinate
J	dimethallyl maleate
K	diallyl urea

Application Example 1

A mixture of 25 g of N-vinyl-2-pyrrolidone, 41.5 g of glycerol, 10.5 g of water, 0.4 g of crosslinking agent A (diethyleneglycol divinyl ether) and 0.25 g of 2-hydroxy-2-methyl-1-phenyl-propanone was cast onto a silicone coated poly (ethylene terephthalate) release liner such as those described in U.S. Patent No. 4,386,135, supported on a glass slide within the space surrounded by two gaskets of poly (tetrafluoroethylene) having a total thickness of 0.86 mm. The mixture was then covered with a quartz plate covered with a second silicone coated poly (ethylene terephthalate) release liner. The plate and slide were clamped together and irradiated with UV light placed at a distance of 35 cm for 10-15 minutes. Obtained gel was clear, extremely tacky and gave clean release from skin.

Application Examples 2-3 and Comparative Examples A-D

Variation of crosslinking agent

Using the method of Example 1, the adhesives shown in Table I were produced using the components shown below.

Table I

Example	N-vinyl-2-pyrrolidone (g)	glycerol (g)	water (g)	photo initiator (g)	crosslinking agent (g)
2	5.0	8.3	2.1	0.05	A(0.05)
3	5.0	8.3	2.1	0.05	B(0.05)
A	5.0	8.3	2.1	0.05	E(0.08)
B	5.0	8.3	2.1	0.05	F(0.09)
C	5.0	8.3	2.1	0.05	G(0.05)
D	5.0	8.3	2.1	0.05	G(0.15)

In each example, the thickness of the adhesive layer was 34 mil.

Excellent adhesives was obtained from examples 2 and 3 and observed to be able to be removed easily and cleanly from the human skin. The adhesive obtained from Comparative Example A was very tacky and left a slight residue on the skin. The adhesive from Comparative Example B was very tacky and adhered to the release liner and tended to be stringy. The adhesive from Comparative Example C showed clean and good tackiness however, it left slight residue on the skin. The adhesive from Comparative Example D was slightly milky, stiffer, flowed under tensile deformation, did not separate cleanly and left a substantial amount of residue.

Application Example 4-7

Using the method and amounts of Example 2, the amount of crosslinking agent A (diethyleneglycol divinyl ether) was changed while maintaining other variables constant in order to examine the variation of properties of the adhesive as shown in Table 2.

Table II

Example	crosslinking agent(g)	Properties of adhesive
4	0.025	clear adhesive, soft & tacky, stringy release
5	0.05	clear adhesive, very tacky, clean release
6	0.10	clear adhesive, very tacky clean release (slightly better than Example 5)
7	0.20	slightly less tackiness, slightly stiffer than Example 5 and 6

Application Example 8 and 9

Adhesive with increased water content

Reactive mixture which was made of one glass plate (lower) and one quartz plate (upper) covered with poly coated with silicone releasing agent, gasket of about 34 mil total thickness which surrounds area of 594 m^2, with two layers, of concentric poly (tetrafluoroethylene) is filled in. (*translator's note: some part is missing from this sentence.)

A piece of hexagonally patterned scrim of polypropylene was placed in the reaction mixture before irradiation with UV light. The apparatus was irradiated from the top for 15 minutes with UV light at a distance of about 30 centimeters. The mixtures are shown in Table III. The photoinitiator was 2-hydroxy-2-methyl-1-phenyl-1-propanone.

Table III

Example	N-vinyl-2-pyrrolidone(g)	glycerol (g)	water (g)	photo initiator (g)	crosslinking agent (g)
8	80	91.2	75.2	0.8	C (0.18)
9	40	45.6	34.6	0.4	A (0.8)

Although the obtained pressure sensitive adhesive gel was very tacky, release from the skin was clean.

Application Example 10. to 18

Adhesives produced in these application example were tested by using belt coating machine at various web speed. Two layered, releasing agent covered poly (ethylene terephthalate) was provided on the moving air-cooled web, then the mixture which was supposed to be polymerized between the layers was covered with knife. This layered composition was brought to the line of fluorescent lamp of which 90 % emission light was between 300 and 400 nanometers. (In example 12, only half of the lamp in the apparatus were operated.)

A 30 mil thick adhesive layer was obtained. The intensity of light was measured by a light meter (Dynachem UV integrating Radiometer Model 500, Dyhachem Corp, Tustin , CA). Web speed is shown in IV on a relative basis. In this case, 400 is equivalent to 5.6 feet per minute
and when it went down to 50, it is equivalent to 0.7 feet per minute.

Produced various adhesives are shown in Table IV. Used photo initiator was 2-hydroxy-2-methyl-1-phenyl-1-propanone.

Table IV

Example	N-vinyl-2-pyrrolidone(g)	glycerol (g)	water (g)	photo initiator(g)	crosslinking agent(g)	web speed
10	32.5	54	13.7	0.32	C (0.13)	400
11	32.5	54	13.7	0.32	C (0.13)	200
12	32.5	54	13.7	0.32	C (0.13)	400
13	100	166	42	1.0	A (1.6)	400
14	100	166	42	1.0	A (1.6)	200
15	100	166	42	1.0	A (1.6)	100
16	100	166	42	1.0	A (1.6)	50
17	16	26	6.8	0.32	A (0.26)	400
18	6	26	6.8	0.32	A (0.26)	100

By the composition of Example 10,11 and 12 , adhesives which are clear and very tacky and yet release cleanly from human skin without leaving any residue, are obtained. Compositions obtained from Example 13 and 14 provided clear and tacky adhesives which released in stringy form. Adhesive in Example 15 is clear and tacky and yet does not leave any residue. Adhesives in Example 17 and 18 are clear, tacky and released in stringy form.

Application Example 19

A mixture of 5.0 g of N-vinyl-2-pyrrolidone, 8.3 g of glycerol, 2.1 g of water, 0.005 g of crosslinking agent D (3,3'-ethylidene bis-(N-vinyl-2-pyrrolidone)) and 0.05 g of 2-hydroxy-2-methyl-1-phenyl-1-propanone was photolyzed by the method of Example 1 and a clear gel was obtained.

Application Example 20

A mixture of 5 g N-vinyl-2-pyrrolidone, 8.3 g of glycerol, 2.1 g of water, 0.005 g of crosslinking agent H (diallyl maleate) and 0.05 g of 2-hydroxy-2-methyl-1-phenyl-1-propanone was photolyzed by the method of Example 1. A clear tacky gel which released cleanly from skin was obtained.

Application Example 21

Example 20 was repeated with the exception that 0.010 g of crosslinking agent I (diallyl succinate) was substituted for the 0.005 g of crosslinking agent H. Clear and tacky gel which released cleanly from skin was obtained.

Application Example 22

Example 20 was repeated with the exception that 0.010 g of crosslinking agent J (dimethallyl maleate) was substituted for 0.005 g of crosslinking agent H. Clear and tacky gel which released cleanly from skin was obtained.

Application Example 23

Example 20 was repeated with the exception that 0.010 g of crosslinking

agent K (1,3-diallylurea) was substituted for 0.005 of crosslinking agent H. Clear and tacky gel which released cleanly from skin was obtained.

Application Example 24

A mixture of 44 g water, 25 g glycerol, 30 g N-vinyl-2-pyrrolidone, 0.15 g 2-hydroxy-2-methyl-1-phenyl1-propanone, 0.052 g 3,3'-ethylidene bis (N-vinyl-2-pyrrolidone) and 1 g pottasium chloride was prepared. A portion of this solution was poured onto a silicone coated release liner covered with a nylon screen material. The sample was left to sit in a nitrogen atmosphere for 1 minute and was phorolyzed for 7 minutes with two sun lamps. The light entered the nitrogen purged chamber through a quartz window from a distance of 12 inches. The obtained gel was very tacky.

Comparative Examples E-H

Experiments were performed by using precursors having different amounts of N-vinyl-2-pyrrolidone (NVP) and acrylic acid (AA) as a comonomer. Instead of using one kind of crosslinking agent of this invention, triethylene glycol bis-methacrylate (TEGBM) was used. Each 100 g precursor contained 1.0 g KCI, 25.5 g H_2O, NaOH (amount sufficient to neutralize 50 % of acid groups), 0.07 g benzildi-methylketal, 0.125 g TEGBM, acrylic acid (AA), N-vinyl-2-pyrrolidone (NVP) and glycerol (remaining balance). The precursor was made by adding KCI to water in a glass container and stirring until the salt was dissolved. Glycerol was added afterwards. In a separate container, the acrylic acid (if used) was mixed with the initiator (benzildimethylketal) and the crosslinking agent (TEGBM). Two kinds of mixtures were mixed and NVP was added right before coating on the substrate. The precursor was coated on a substrate and exposed to ultraviolet radiation until completely polymerized in the nitrogen atmosphere. Immediately after the polymerization, opacity (shows phase separation) and initial tackiness of the composition were measured. Comparative examples E and F showed acceptable tackiness and showed no phase separation. Example G was soft and left a residue when removed from skin. Example H was very soft and left considerable amount of residue when removed from skin.

Table V

Comparative Example	AA (%)	NVP (%)
E	16.87	5.62
F	12.5	12.5
G	6.87	20.62
H	0	30

This invention may be embodied in other specific forms without leaving from its spirit or essential characteristics. The described embodiment should be regarded only as illustrative and not restrictive in all respects. Therefore, the scope of this invention is described by the attached claims rather than by the foregoing description. All changes which come within the meaning and range of equivalency of the claims are to be embraced within their scope.

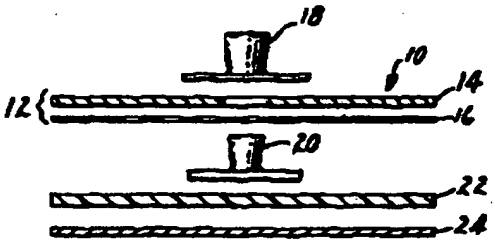
[Brief explanation of the drawings]

Drawing 1 is a cross sectional drawing of a disposable ECG electrode containing the conductive adhesive of this invention.

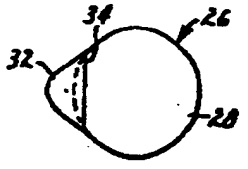
Drawing 2 is a upper plan of the other form ECG electrode of the drawing 1.

Drawing 3 is a cross sectional drawing of the electrode of the drawing 2.

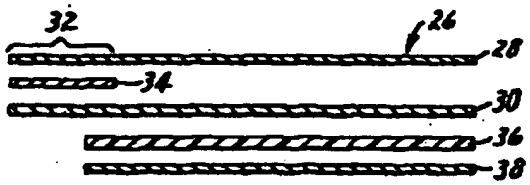
[Figure 1]



[Figure 2]



[Figure 3]



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	JKK		JKZ		
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*Translator's note: There are several obvious mistakes in this patent. I marked them with symbol *.*

Translated by Sayuki Sugimura, 651-490-0233,ssugimura@pipeline.com, March 11, 2001